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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,740	12/01/2006	Bernard Freiss	3493-0179PUS1	5296
2292 7590 12/23/2008 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747				
EXAMINER				
LAU, JONATHAN S				
ART UNIT		PAPER NUMBER		
1623				
NOTIFICATION DATE		DELIVERY MODE		
12/23/2008		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

# Office Action Summary

**Application No.**

10/594,740

**Applicant(s)**

FREISS ET AL.

**Examiner**

Jonathan S. Lau

**Art Unit**

1623

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 11-21 and 26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-21 and 26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Office Action is responsive to Applicant's Amendment and Remarks, filed 14 Oct 2008, in which claims 12 and 21 are amended to change the scope and breadth of the claim and new claim 26 is added.

This application is the national stage entry of PCT/FR05/00739, filed 29 Mar 2005; and claims benefit of foreign priority document FRANCE 0403450, filed 01 Apr 2004, and foreign priority document FRANCE 0411201, filed 21 Oct 2004; currently English language translations of these foreign priority document have not been filed.

Claims 11-21 and 26 are pending.

### ***Rejections Withdrawn***

Applicant's Amendment, filed 14 Oct 2008, with respect to claims 12 and 21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite has been fully considered and is persuasive, as amended claim 12 does not recite a broad range or limitation together with a narrow range or limitation and amended claim 21 specifies the weight of which the diffusion agent is a percentage weight.

This rejection has been **withdrawn**.

The following are modified grounds of rejection necessitated by Applicant's Amendment, filed 14 Oct 2008, in which claims 12 and 21 are amended to change the scope and breadth of the claim and new claim 26 is added.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Amended Claims 11-21 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006) as evidenced by Van Hees et al. 1999 (Pharmaceutical Research, 1999, 16, p1864-1870, provided by Applicant on IDS filed 29 Sep 2006) and in view of Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, cited in PTO-892).

Van Hees et al. 2002 discloses preparing complexes of piroxicam and  $\beta$ -cyclodextrin using super-critical CO<sub>2</sub> (SCCO<sub>2</sub>) (page 271, left column, lines 9-10), the inclusion compound of an active substance whose aqueous solubility is poor and a host molecule in a dense pressurized fluid. Van Hees et al. 2002 discloses the process using the technique described in Van Hees et al. 1999 (Van Hees et al. 2002, page 271, right column, lines 6-8), and Van Hees et al. 1999 discloses the process of bringing the active substance, piroxicam, in contact with the host molecule,  $\beta$ -cyclodextrin,

pressurized and exposed to  $\text{SCCO}_2$  in the static mode and recovering the molecular complex formed (Van Hees et al. 1999, page 1865, left column, paragraph Preparation of Inclusion Complexes), meeting limitations in instant claims 11, 12, 15-17. Van Hees et al. 2002 discloses the addition of agents for interaction with the complex such as L-lysine, an amino acid that is a base, and the non-preferred aqueous ammonium hydroxide solution (page 273, right column, lines 15-20), as well as the use of citric acid, a carboxylic acid (page 274, right column, line 2), meeting limitations in instant claims 13 and 14. Van Hees et al. 2002 discloses the process performed at pressures between 15-30 and 45 MPa and a temperatures of 125-137 and 150 °C (page 271, right column, paragraph Preparation of complexes using  $\text{SCCO}_2$ ), meeting limitations of instant claim 18. Van Hees et al. 1999 discloses the extraction vessel in the apparatus for performing the molecular diffusion of piroxicam and  $\beta$ -cyclodextrin does not include a stirring mechanism (Van Hees et al. 1999, page 1865, left column, Fig. 1. Schematic diagram of the apparatus), meeting limitations in instant claim 20.

Van Hees et al. 2002 does not specifically disclose the process wherein the molecular diffusion is performed in the presence of one or more diffusion agents (instant claim 11), wherein said diffusion agent is chosen from the group consisting of alcohols, ketones, ethers, esters and water, with or without surfactant, and their mixtures (instant claim 19), or wherein the diffusion agent is added continuously or portionwise in an amount of between 1 and 50% by weight (instant claim 21). Van Hees et al. 2002 does not specifically disclose the process including the step of recovering the active substance/host molecule molecular complex thus formed prior to adding to and mixing

with the active substance/host molecule molecular complex an agent for interaction with the complex and recovering the soluble inclusion compound thus formed (instant claim 11).

Junco et al. teaches the complexation of a pharmaceutically active substance with  $\beta$ -cyclodextrin using super-critical CO<sub>2</sub> (page 69, abstract). Junco et al. teaches the addition of a small amount of co-solvent to a supercritical fluid can have dramatic effects on its solvent power (page 70, left column, lines 4-6). Junco et al. specifically teaches the use of co-solvents ethyl acetate, acetone, methanol, ethanol, 1-propanol and 2-propanol (page 70, left column, lines 6-11). Junco et al. teaches the use of ethanol added continuously in the amount of 4% by weight (page 70, right column, line 17).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the process of preparing complexes of piroxicam and  $\beta$ -cyclodextrin using super-critical CO<sub>2</sub> disclosed by Van Hees et al. 2002 with the addition of a small amount of co-solvent, or diffusion agent, taught by Junco et al. Both Van Hees et al. 2002 and Junco et al. are drawn to the process of preparing complexes of an active agent and  $\beta$ -cyclodextrin using super-critical CO<sub>2</sub>. One of ordinary skill in the art would have been motivated to combine the process disclosed by Van Hees et al. 2002 with teaching of Junco et al. because Junco et al. teaches the solubility enhancement with these co-solvents is considerable (Junco et al. page 70, left column, lines 10-11).

With regard to the process including the step c. of recovering the active substance/host molecule molecular complex thus formed prior to step d. adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex and step e. recovering the soluble inclusion compound thus formed (instant claim 11), MPEP 2144.04 IV. C. states "selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results." Examiner notes that the instant specification, examples 2-5 spanning pages 27-28 make comparison with the process using only aqueous ammonia. Van Hees et al. 2002 discloses supercritical ammonia is extremely corrosive for the extractor, whereas L-lysine and trometamol are not (page 273, right column, lines 18-20). One of ordinary skill in the art would understand that corrosion of the extractor would lead to a less efficient reaction with a lower yield. Therefore the results of the experiments disclosed in the instant specification are neither unexpected nor commensurate with the scope of the claims.

**Response to Applicant's Remarks:**

Applicant's Remarks, filed 14 Oct 2008, have been fully considered and not found to be persuasive.

Applicant remarks that the present invention effectively requires two steps and that the prior art uses a single step process. However, instant claim 11 recites stages a, b, c, d and e. According to the ordinary definition of "stage" (Merriam Webster Online Dictionary, cited in PTO-892), a stage is "a period or step in a process" (entry 5a).

Therefore the finding that the instant invention is obvious over the prior art as the selection of any order of performing process steps is proper.

Applicant remarks that the instant invention produces unexpectedly improved results over the process disclosed in Van Hees (2002). Applicant shows evidence in example 1, the complex of piroxicam and cyclodextrin. However, this evidence is not commensurate in scope with the instant claims, drawn to a host molecule and an active substance not being very soluble in an aqueous medium (instant claim 11). Therefore this evidence is not persuasive with regard to the scope of the invention as claimed.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).



Amended Claims 11-22 and 26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 13 of copending Application No. 10/554,058 in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006). Both instant claims 11-22 and claims 1-10 and 13 of copending Application No. 10/554,058 are drawn to the process of preparation of a soluble inclusion compound by bringing the active substance into contact with a host molecule in static mode and carrying out molecular diffusion in a dense pressurized fluid such as super-critical CO<sub>2</sub>.

Claims 1-10 and 13 of copending Application No. 10/554,058 do not specifically disclose adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex.

Van Hees et al. 2002 teaches as above. Van Hees et al. 2002 teaches the inclusion yield is significantly higher when a ternary alkaline substance such as L-lysine, or an agent for interaction with the complex, is added (page 274, left column, lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the process disclosed in Claims 1-10 and 13 of copending Application No. 10/554,058 with adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex as taught by Van Hees et al. 2002. One of ordinary skill in the art would be motivated to combine the process disclosed in Claims 1-10 and 13 of copending Application No. 10/554,058 with the teachings of Van Hees et al. 2002 because Van Hees et al. 2002 teaches the

inclusion yield is significantly higher when a ternary alkaline substance, or agent for interaction with the complex, is added.

This is a provisional obviousness-type double patenting rejection.

**Response to Applicant's Remarks:**

Applicant's Remarks, filed 14 Oct 2008, have been fully considered and not found to be persuasive.

Applicant remarks that the present invention effectively requires two steps and that the prior art uses a single step process. However, instant claim 11 recites stages a, b, c, d and e. According to the ordinary definition of "stage" (Merriam Webster Online Dictionary), a stage is "a period or step in a process" (entry 5a). Therefore the finding that the instant invention is obvious over the prior art as the selection of any order of performing process steps is proper.

Applicant remarks that the instant invention produces unexpectedly improved results over the process disclosed in Van Hees (2002). Applicant shows evidence in example 1, the complex of piroxicam and cyclodextrin. However, this evidence is not commensurate in scope with the instant claims, drawn to a host molecule and an active substance not being very soluble in an aqueous medium (instant claim 11). Therefore this evidence is not persuasive with regard to the scope of the invention as claimed.

As this provisional obviousness-type double patenting rejection is not the only remaining grounds of rejection, it is proper to maintain this modified provisional rejection.

Amended Claims 11-21 and 26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 8-14 of copending Application No. 10/492,346 in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006). Instant claims 11-22 and claims 1 and 8-14 of copending Application No. 10/492,346 are drawn to the process of preparation of a soluble inclusion compound by bringing the active substance into contact with a host molecule, or porous support, such as cyclodextrin, in static mode and carrying out molecular diffusion in a dense pressurized fluid such as super-critical CO<sub>2</sub>.

Claims 1 and 8-14 of copending Application No. 10/492,346 do not specifically disclose adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex.

Van Hees et al. 2002 teaches as above. Van Hees et al. 2002 teaches the inclusion yield is significantly higher when a ternary alkaline substance such as L-lysine, or an agent for interaction with the complex, is added (page 274, left column, lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the process disclosed in Claims 1-10 and 13 of copending Application No. 10/554,058 with adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex as taught by Van Hees et al. 2002. One of ordinary skill in the art would be motivated to combine the process disclosed in Claims 1-10 and 13 of copending Application No. 10/554,058 with the teachings of Van Hees et al. 2002 because Van Hees et al. 2002 teaches the

inclusion yield is significantly higher when a ternary alkaline substance, or agent for interaction with the complex, is added.

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As this provisional obviousness-type double patenting rejection is not the only remaining grounds of rejection, it is proper to maintain this modified provisional rejection.

***Conclusion***

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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